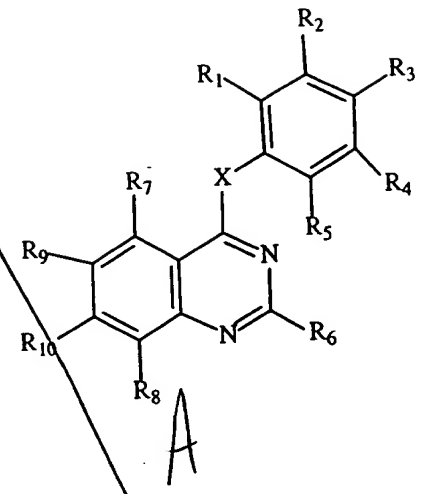
Claims

What is claimed is:

1. A compound of formula I:



wherein:

X is HN, $R_{11}N$, S, O, CH_2, or $R_{11}CH$;

R_{11} is hydrogen, $(C_1\text{-}C_4)$alkyl, or $(C_1\text{-}C_4)$alkanoyl;

R_1-R_8 are each independently hydrogen, hydroxy, mercapto, amino, nitro, $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$alkylthio, or halo; wherein two adjacent groups of R_1-R_5 together with the phenyl ring to which they are attached may optionally form a fused ring, for example forming a naphthyl or a tetrahydronaphthyl ring; and further wherein the ring formed by the two adjacent groups of R_1-R_5 may optionally be substituted by 1, 2, 3, or 4 hydroxy, mercapto, amino, nitro, $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$alkylthio, or halo; and

R_9 and R_{10} are each independently hydrogen, $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy, halo, or $(C_1\text{-}C_4)$alkanoyl; or R_9 and R_{10} together are methylenedioxy; or a pharmaceutically acceptable salt thereof;

provided the compound is not 4-(4′-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline.

2. The compound of claim 1 wherein X is $R_{11}N$.

3. The compound of claim 1 wherein X is HN.

4. The compound of claim 1 wherein each of R_1, R_2, R_4, R_5, R_6, R_7, and R_{10} is H.

5. The compound of claim 1 wherein R_3 is $(C_1$-$C_4)$alkoxy, hydroxy, nitro, halo, trifluoromethyl, or $NR_{12}R_{13}$ wherein R_{12} and R_{13} are each independently hydrogen, $(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkenyl, $(C_1$-$C_4)$alkynyl, $(C_3$-$C_8)$cycloalkyl, or heterocycle.

6. The compound of claim 1 wherein R_3 is hydroxy.

7. The compound of claim 1 wherein R_2 or R_3 is hydroxy.

8. The compound of claim 1 wherein R_2 or R_3 is hydroxy; and one of R_1-R_5 is halo.

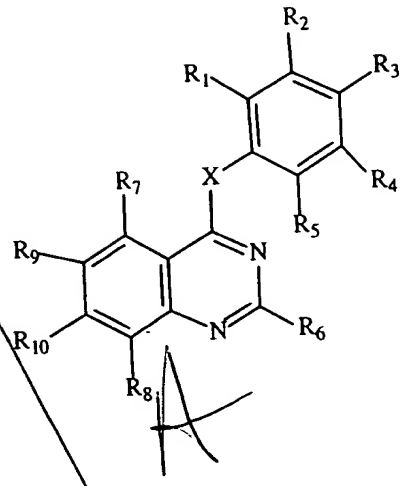
9. The compound of claim 1 wherein R_2 or R_3 is hydroxy.

10 The compound of claim 1 wherein R_8 is $(C_1$-$C_4)$alkoxy.

11. The compound of claim 1 wherein R_9 is $(C_1$-$C_4)$alkoxy.

12. The compound of claim 1 which is 4-(3′-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline; 4-(3',5'-dibromo-4′-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline or 4-(3'-bromo-4′-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline; or a pharmaceutically acceptable salt thereof .

13. A pharmaceutical composition comprising a compound of formula I:



wherein:

X is HN, $R_{11}N$, S, O, CH_2, or $R_{11}CH$;

R_{11} is hydrogen, (C_1-C_4)alkyl, or (C_1-C_4)alkanoyl;

R_1-R_8 are each independently hydrogen, hydroxy, mercapto, amino, nitro, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkylthio, or halo; wherein two adjacent groups of R_1-R_5 together with the phenyl ring to which they are attached may optionally form a fused ring, for example forming a naphthyl or a tetrahydronaphthyl ring; and further wherein the ring formed by the two adjacent groups of R_1-R_5 may optionally be substituted by 1, 2, 3, or 4 hydroxy, mercapto, amino, nitro, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, (C_1-C_4)alkylthio, or halo; and

R_9 and R_{10} are each independently hydrogen, (C_1-C_4)alkyl, (C_1-C_4)alkoxy, halo, or (C_1-C_4)alkanoyl; or R_9 and R_{10} together are methylenedioxy; or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

14. The composition of claim 13 wherein R_2 or R_3 is hydroxy.

15. The composition of claim 13 wherein R_2 or R_3 is hydroxy; and one of R_1-R_5 is halo.

16. The composition of claim 13 wherein the compound of formula I is 4-(3'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline; 4-(3',5'-dibromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline or 4-(3'-bromo-4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline; or a pharmaceutically acceptable salt thereof .

17. A pharmaceutical composition comprising 4-(4'-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline; or a pharmaceutically acceptable salt thereof ; and a pharmaceutically acceptable carrier.

18. A therapeutic method for treating leukemia or lymphoma in a mammal comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

19. A therapeutic method for treating or preventing organ transplant rejection in a mammal comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

20. A therapeutic method for preventing or reducing ultraviolet B radiation-induced inflammatory response in a mammal comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

21. A therapeutic method for inhibiting the release of prostaglandin E_2 in a mammal comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

22. A therapeutic method for preventing or reducing UVB-induced skin edema or vascular permeability changes in a mammal comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

23. A therapeutic method for preventing or reducing ultraviolet B radiation-induced damage to epithelial cells or mutation frequency in skin in a mammal comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

24. A therapeutic method for protecting a mammal from tumorigenic effects of UVB light comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

25. A therapeutic method for inhibiting T-cell activity in a mammal comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

26. A therapeutic method for preventing or treating an autoimmune disease comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

27. A therapeutic method for preventing or treating graft-verses host disease comprising administering to the mammal in need thereof an effective amount of a JAK-3 inhibitor.

28. The method of any one of claims 18-27 wherein the compound is a compound of claim 1.

29. The method of any one of claims 18-27 wherein the JAK-3 inhibitor is 4-(4′-hydroxyl-phenyl)-amino-6,7-dimethoxyquinazoline; or a pharmaceutically acceptable salt thereof.

Add A1

add D3